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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,972	10/01/2004	Yusheng Xiong	2111YP	9958

210 7590 11/30/2007

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EXAMINER	
CHUNG, SUSANNAH LEE	
ART UNIT	**PAPER NUMBER**
1626	
MAIL DATE	**DELIVERY MODE**
11/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,972	XIONG ET AL.	
	Examiner	Art Unit	
	Susannah Chung	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1 and 4-9* is/are allowed.

6)☒ Claim(s) *10-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 4-15 are pending in the instant application. Claims 2-3 are canceled. Claims 10-15 are withdrawn.

Response to Non-Final Office Action

Response and Amendment of Claims

Acknowledgment is made of applicant's response and amendment of the claims filed on 10/17/2007.

Claims 1-4 were rejected under 35 USC 102(b) and 103(a) as being anticipated or obvious over the prior art. In view of the amendment to the claims, the rejections are withdrawn.

Rejoinder

Claims 1 and 4 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 10-15, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on 4/9/2007 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction

requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in MPEP 2164.01(a), "there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

The factors to be considered when determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, were described in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as:

1. the nature of the invention;
2. the breadth of the claims;
3. the state of the prior art;
4. the relative skill of those in the art;
5. the predictability or unpredictability of the art;
6. the amount of direction or guidance presented [by the inventor];

7. the presence or absence of working examples; and

8. the quantity of experimentation necessary [to make and/or use the invention].

The eight Wands factors are applied to Claims 10-15 of the present invention below:

(1) The Nature of the Invention

Claims 10-15 are directed to a method of inhibiting activity of lethal factor (LF) released from bacterial in a mammal, the method comprising administering to a patient in need thereof a therapeutically effective amount of a compound of formula (I).

(2) The Breadth of the claims

Claims 10-15 will be give its broadest reasonable interpretation. The applicable rule for interpreting the claims is that "each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." See MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). In view of this rule, Claims 10-15, which do not specify the many possible diseases that could be described by the term "inhibiting activity of lethal factor from bacterial in a mammal" will be interpreted to encompass all types of diseases that could be described by the term "inhibiting activity of lethal factor from bacterial in a mammal."

(3) The state of the prior art

The state of the art at the time of this application was that lethal factor is a zinc-dependent metalloprotease that appears to exert toxic affect by cleaving mitogen-activated protein kinase kinases. Lethal factor has been shown to cleave synthetic peptides *in vitro*. It is also known to be an enzymatic component of the anthrax toxin. The anthrax toxin consists of three proteins: a receptor-binding component designated protective antigen and two enzymatic

components termed edma factor and lethal factor. Anthrax is an infectious disease of warm-blooded animals cause by a spore forming bacterium (bacillus anthracis). Antibiotics are known to kill bacillus anthracis and other bacteria known to cause anthrax.

(4) The relative skill of those in the art

The level of skill in the art (pharmaceutical chemists, physicians) would be high.

(5) The predictability or unpredictability of the art

It is noted that the pharmaceutical art generally is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement varies inversely with the degree of unpredictability in the factors involved. In re Fisher, 427 F.2d 833, 839. Therefore, the more unpredictable an area, the more specific enablement is needed in order to satisfy the statute. Added to the unpredictability of the art itself is the question whether in vitro activity against synthetic peptides by one of the compound of the present invention could be reliably and predictably extrapolated to in vivo activity in patients infected with anthrax or bacillus anthracis. There is no absolute predictability, even in view of the high level of skill in the art.

(6) The amount of direction or guidance presented (by the inventor)

The specification in the present invention incorporates by reference an assay showing that the instantly claimed compounds are potential lethal factor inhibitors. (See specification page 32, Assay for determining lethal factor inhibition by Cummings et al.) It is the assertion of the instant specification that inhibition of lethal factor alone could treat or prevent anthrax.

(7) The presence or absence of working examples

The lethal factor enzyme binding assay IC50 results for two exemplary compounds range from 15uM or less. (See specification page 33). However, the specification has no working examples, such as in vivo or in vitro studies of the role of the instantly claimed compounds as lethal factor inhibitors, which in turn treat or prevent anthrax or bacillus anthracis.

(8) The quantity of experimentation necessary (to make and/or use the invention)

Given the absence of direction or guidance (or working examples) in the specification for the role of the compounds of formula (I) in the treatment or prevention of anthrax, it would cause a skilled artisan an undue amount of experimentation to practice this invention to determine which patients whether inhibition of lethal factor alone could treat or prevent anthrax. The anthrax toxin consists of three proteins: a receptor-binding component designated protective antigen and two enzymatic components termed edma factor and lethal factor. The instant specification does not support the assertion that inhibition of lethal factor alone could treat anthrax. Currently, claims 10-15 read on the inhibition of lethal factor from all bacterial strains, but the specification only supports bacillus anthracis. Therefore, claims are not enabled for inhibiting the activity of lethal factor released from bacterial in a mammal.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular the term "released" found in line 2 of claim 10 is indefinite because the mechanism by which the release of the "inhibiting activity of lethal factor" is not described.

Claims 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "pharmaceutically acceptable salts " renders the claim confusing because one skilled in the art would not know if the salt form of the compound would also have to be present in conjunction with the compound itself. It is suggested that "pharmaceutically acceptable salt" be adopted.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Line 1 currently reads "the method according to claim 10, wherein said administering..." A word or phrase is missing after the word "said." In addition, it is unclear whether the conjunction "or" (in the second to last line) should appear before the last item in the list or if "N-acylated amino acids" is an example of a "metabolizing enzyme."

Claim 15 contains the trademark/trade name "PRIMAXIN®." Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a type of cilastatin and, accordingly, the identification/description is indefinite.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

A telephone call was placed to Attorney Julie Lake on 11/14/207 and a written action was requested.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Chung whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLC

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Date: 15 November 2007